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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/865,291	05/24/2001	Roger Y. Tsien	UC089.1CPC1CP1	5198

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MAR 29 2004

HELLER EHRMAN

EXAMINER

KAPUST, RACHEL B

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

HEWM LLP - SV Office

Description

Due/Rmr

Final/Deadline

Initials

RESPONSE TO OA
6/25/04
9/25/04
DZ1

Office Action Summary <div style="position: relative; height: 40px;"> <div style="position: absolute; top: 0; left: 0; right: 0; background-color: black; color: white; text-align: center; font-weight: bold; font-size: 1.2em;">RECEIVED</div> <div style="position: absolute; bottom: 0; left: 0; right: 0; background-color: black; color: white; text-align: center; font-weight: bold; font-size: 1.2em;">MAR 29 2004</div> </div>	Application No. 09/866,291 Examiner Rachel B. Kapust	Applicant(s) TSIEN ET AL. <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%;">Art Unit</td> <td style="width: 50%;"></td> </tr> <tr> <td>1647</td> <td></td> </tr> </table>	Art Unit		1647	
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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply HELLER EHRMAN

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 02 June 2003.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 95,106,108-121,125,128,130,131 and 145-163 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 95,106,108-121,125,128,130,131 and 145-163 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on 24 May 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some * c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>10</u> .	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6) <input type="checkbox"/> Other: _____.
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DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the embodiment comprising a polynucleotide encoding a chimeric phosphorylation indicator, where the chimeric phosphorylation indicator comprises, in operative linkage, a donor molecule, a phosphorylatable domain, a phosphoaminoacid binding domain, and an acceptor molecule, wherein said donor molecule comprises amino acids 1-227 of SEQ ID NO: 6, said phosphorylatable domain comprises SEQ ID NO: 23, said phosphoaminoacid binding domain comprises a Src homology domain-2, and said acceptor molecule comprises citrine (SEQ ID NO: 10) is acknowledged. The traversal is on the ground(s) that all of the chimeric phosphorylation indicators of the current application have a donor molecule, a phosphorylatable domain, a phosphoaminoacid binding domain, and an acceptor molecule, thus the different embodiments are not patentably distinct.

Applicant's arguments have been fully considered and have been found to be persuasive. Claims 95, 106, 108-121, 125, 128, 130, 131, and 145-163 will be examined in view of the particularized chimeric phosphorylation indicator as represented by claim 95 and in view of the generic chimeric phosphorylation indicator as represented by claim 147.

Claims 95, 106, 108-121, 125, 128, 130, 131, and 145-163 are under consideration.

Priority

It is noted that in the response dated March 17, 2003, Applicants brought to the attention of the Examiner that on August 16, 2002 a supplemental application data sheet was filed which expressly rescinded any claims to benefits of priority under 35 U.S.C. 120.

Specification

The use of the trademarks QUICKCHANGE™ (p. 48), B-PER™ (p. 48), COMPLETE™ (p. 49), MICROCON™ (p. 49), CENTRICON™ (p. 49), METAFUOR™ (p. 51), and EFFECTENET™ (p. 58) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

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Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 95, 106, 108-121, 125, 128, 130, 131, 145, 146, 149-156, and 161-163 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 95 is drawn to a polynucleotide encoding a chimeric phosphorylation indicator, wherein the acceptor molecule encodes the amino acid sequence of SEQ ID NO: 10 having "Q69M". The amino acid at position 69 of SEQ ID NO: 10 is a leucine and not a methionine. It is not clear whether SEQ ID NO: 10 is incorrect or whether the glutamine to methionine mutation occurs at another position. Claims 106, 108-121, 125, 128, 130, 131, 145, 146, 149-156, and 161-163 are rejected as being dependent on claim 95.

Claim 108 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 108 is drawn to a polynucleotide encoding a polypeptide having mutations of either A206K, L221K, F223R or L221K and F223R in either SEQ ID NO: 6 or 10. The amino acids at positions 206 and 223 of SEQ ID NOS: 6 and 10 are serine and glutamic acid, respectively. Again, it is not clear whether SEQ ID NOS: 6 and 10 are incorrect or whether the mutations occur at other positions.

Claims 147-148 and 153-160 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 147 and 153 are dependent on cancelled claim 132.

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Claim 157 is dependent on cancelled claim 138. Claims 148, 154-156, and 158-160 are rejected as being dependent on claims 147, 153, or 157. Appropriate correction is required.

Claims 150-152, 154-156, and 158-160 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 150, 154, and 158 are drawn to polynucleotides encoding "different chimeric phosphorylation indicators". It is not clear whether the claims are meant to include chimeric phosphorylation indicators that are different from that of claim 95 or whether the chimeric phosphorylation indicators are meant to be different from each other, i.e. no two chimeric phosphorylation indicators are the same. Similarly, claims 151, 155, and 159 are drawn to polynucleotides encoding "different phosphorylation domains" and "different phosphorylatable polypeptides" and "different phosphorylatable domains". It is not clear whether the claims are meant to include only polynucleotides encoding domains different from that of claim 95, or whether the claims are meant to include all phosphorylatable domains so long as no two are the same. Claims 152, 156, and 160 are drawn to polynucleotides encoding "different donor molecule or acceptor molecules or both" or "different fluorescent proteins". Again, it is not clear whether the claims are meant to include only polynucleotides encoding fluorescent proteins that are different from that of claim 95 or whether the polynucleotides can encode any fluorescent protein so long as no two are the same.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002

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do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 147-149, 153, and 157 are rejected under 35 U.S.C. 102(e) as being anticipated by Craig *et al.* (U.S. Patent No. 6,656,696). Claims 147-160 are drawn to polynucleotides encoding chimeric phosphorylation indicators, wherein the indicator comprises a phosphorylatable polypeptide and a fluorescent protein. The claims are also drawn to kits comprising the polynucleotides. Craig *et al.* teach polypeptides comprising a blue fluorescent protein donor, a green fluorescent protein acceptor, a site for phosphorylation or dephosphorylation, and a phosphorylation- or dephosphorylation-dependent binding domain (column 19, lines 23-38 and column 21, line 20 through column 22, line 48). Craig *et al.* teach the use of the polypeptide for monitoring the activity of protein kinases or phosphatases (column 5, lines 4-5). Craig *et al.* teach nucleic acid vectors for the expression of the polypeptides (column 30, line 50 through column 31, line 57). Craig *et al.* teach kits for assaying the activity of protein kinases or phosphatases (columns 35 and 36). Thus, claims 147-149, 153, and 157 are anticipated by Craig *et al.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

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3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 150-152, 154-156, and 158-160 are rejected under 35 U.S.C. 103(a) as being unpatentable over Craig et al. Claims 150-152, 154-156, and 158-160 are drawn to kits comprising a plurality of polynucleotides encoding different chimeric phosphorylation indicators. Craig et al. teach kits comprising a chimeric phosphorylation indicator, but they do not teach kits comprising a plurality of indicators or kits comprising different chimeric phosphorylation indicators. However, it would have been obvious to a person of ordinary skill in the art to modify the kits as taught by Craig et al. to include a plurality of different phosphorylation indicators in the kits. Motivation to do so is provided by Craig et al. who teach that any protein which fluoresces when excited may be used and any phosphorylation-dependent binding domain may be used. , because there is a need in the art for efficient means of monitoring and/or modulating post-translational protein phosphorylation and/or dephosphorylation.

Conclusion

NO CLAIMS ARE ALLOWED.

The following articles, patents, and published patent applications were found by the Examiner during the art search while not relied upon are considered pertinent to the instant application:

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel B. Kapust whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RBK
3/19/04


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